

FILE 'MEDLINE, DRUGU, EMBASE, USPATFULL' ENTERED AT 13:43:33 ON 05 SEP  
2002

|     |            |                            |
|-----|------------|----------------------------|
| L2  | 0 S        | 126613-39-6                |
| L3  | 0 S        | 126613-39-6                |
| L4  | 0 S        | 126613-39-6                |
| L5  | 0 S        | 126613-39-6/REG            |
| L6  | 41 S       | COMPER                     |
| L7  | 0 S        | 126613-39-6                |
| L8  | 4335 S     | 87333-19-5                 |
| L9  | 162 S      | L8 AND (RENAL DISEASE)     |
| L10 | 18 S       | L9 AND ALBUMIN             |
| L11 | 15 DUP REM | L10 (3 DUPLICATES REMOVED) |

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS

RN 87333-19-5 REGISTRY

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(R\*)],2.alpha.,3a.beta.,6a.beta.]]-

OTHER NAMES:

CN Altace

CN HOE 498

CN **Ramipril**

CN Tritace

FS STEREOSEARCH

DR 126613-39-6

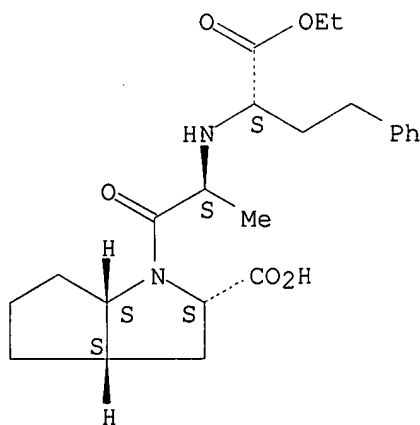
MF C23 H32 N2 O5

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSNB, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK\*, MSDS-OHS, PHAR, PHARMASEARCH, PROMT, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL  
(\*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

633 REFERENCES IN FILE CA (1967 TO DATE)

13 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

634 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=>

L11 ANSWER 11 OF 15 MEDLINE

DUPLICATE 2

AB Angiotensin-converting enzyme inhibitors reduce proteinuria in both normotensive and hypertensive patients with proteinuric **renal disease**. However, the mechanism of the antiproteinuric effect has not been clarified. We performed a prospective, double-blind, placebo-controlled, randomized crossover trial to test the hypothesis that the antiproteinuric effect of ramipril was due to an improvement in glomerular permselectivity independent of blood pressure and glomerular filtration rate. The effect of low-dose (1.25 mg/d) and high-dose (5 mg/d) ramipril was assessed in 15 normotensive nondiabetic patients with proteinuria (> 150 mg/d). The study was divided into four 12-week periods: placebo, high- or low-dose ramipril, crossover to low- or high-dose ramipril, and placebo. Blood pressure, glomerular filtration rate, renal plasma flow rate, urinary protein excretion rate, and plasma angiotensin II levels were measured at the end of each period. Mean arterial pressure, urine protein to creatinine ratio, and **albumin** excretion rate decreased significantly during low- and high-dose ramipril. Glomerular filtration rate and renal plasma flow rate were not changed significantly. Plasma angiotensin II levels decreased with both low- and high-dose ramipril. There were no episodes of hypotension and only one subject developed cough during ramipril that did not require discontinuation of the study drug. In conclusion, administration of ramipril in both low and high doses lowered blood pressure and reduced proteinuria in this cohort of normotensive patients with a variety of proteinuric **renal diseases**. The antiproteinuric effect of ramipril is probably mediated by a reduction in glomerular capillary pressure.

L11 ANSWER 13 OF 15 MEDLINE

AB Microalbuminuria predicts early mortality and **renal disease** in non-insulin-dependent diabetic patients. In insulin-dependent diabetic patients, angiotensin converting enzyme inhibition decreases microalbuminuria and retards the progression of **renal disease**. The aim of this study was to evaluate the effect of low dose ramipril on **albumin** excretion rate (AER) and blood pressure in non-insulin-dependent diabetic patients with persistent microalbuminuria (AER > 20 < 200 micrograms/min) and normal blood pressure or mild hypertension. The study was a randomized, double-blind, placebo-controlled clinical trial of 6 months duration at 14 hospital-based diabetes centers in northeastern Italy. Blood pressure, plasma glucose, and body weight were determined every month; AER, serum creatinine, glycosylated hemoglobin, and plasma lipids at baseline, after 1 month, and at the end of the study. Of 122 non-insulin-dependent diabetic patients randomly allocated in blocks of four to receive either ramipril (1.25 mg/day) or placebo, 108 (54 in the ramipril group and 54 in the placebo group) completed the study. At baseline, age, duration of diabetes, body mass index, and glycosylated hemoglobin were similar in the two groups and remained unchanged throughout the study. In the placebo group, AER rose from a baseline median of 65 micrograms/min (range 53 to 76, 95% confidence Interval) to 72 micrograms/min (57 to 87) and to 83 micrograms/min (62 to 104) after 1 and 6 months, respectively, but fell from 62 micrograms/min (48 to 76) to 45 micrograms/min (33 to 57) and to

Journal code: 8110075. ISSN: 0272-6386.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
(RANDOMIZED CONTROLLED TRIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199701  
ENTRY DATE: Entered STN: 19970128  
Last Updated on STN: 19970128  
Entered Medline: 19970115

=> d ibib 13

L11 ANSWER 13 OF 15 MEDLINE  
ACCESSION NUMBER: 96051093 MEDLINE  
DOCUMENT NUMBER: 96051093 PubMed ID: 8541002  
TITLE: Effect of low-dose ramipril on microalbuminuria in  
normotensive or mild hypertensive non-insulin-dependent  
diabetic patients. North-East Italy Microalbuminuria Study  
Group.  
AUTHOR: Trevisan R; Tiengo A  
CORPORATE SOURCE: Unit for Metabolic Diseases, University of Padua, Italy.  
SOURCE: AMERICAN JOURNAL OF HYPERTENSION, (1995 Sep) 8 (9) 876-83.  
Journal code: 8803676. ISSN: 0895-7061.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
(MULTICENTER STUDY)  
(RANDOMIZED CONTROLLED TRIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199602  
ENTRY DATE: Entered STN: 19960227  
Last Updated on STN: 19960227  
Entered Medline: 19960214

*Adonis*

=> d ibib 14

L11 ANSWER 14 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 93203530 EMBASE  
DOCUMENT NUMBER: 1993203530  
TITLE: Monitoring diabetic nephropathy: Glomerular filtration  
rate  
and abnormal albuminuria in diabetic **renal**  
**disease** - Reproducibility, progression, and  
efficacy of antihypertensive intervention.  
AUTHOR: Mogensen C.E.; Hansen K.W.; Nielsen S.; Pedersen M.M.;  
Rehling M.; Schmitz A.  
CORPORATE SOURCE: Med. Dept. M Diabetes/Endocrinology, Aarhus  
Kommunehospital, University Hospitals, DK-8000 Aarhus C,  
Denmark  
SOURCE: American Journal of Kidney Diseases, (1993) 22/1  
(174-187).  
ISSN: 0272-6386 CODEN: AJKDDP  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Conference Article  
FILE SEGMENT: 006 Internal Medicine

53 micrograms/min (38 to 69), respectively, in the ramipril group, a significant difference between the groups ( $P < .01$ ). (ABSTRACT TRUNCATED

AT

250 WORDS)

L11 ANSWER 14 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AB The principal end point in the evaluation of treatment in incipient and overt diabetic nephropathy is rate of decline in glomerular filtration rate (GFR). Therefore, information on reproducibility of GFR measurements is essential in the planning and evaluation of clinical trials. We studied

reproducibility of GFR measurements in insulin-dependent and non-insulin-dependent diabetes mellitus patients using, respectively, a constant-infusion technique with urine collection and labeled iothalamate as a tracer marker and a single-shot procedure using Cr-EDTA, measuring the

GFR

from the decline in plasma level after bolus injection. The coefficient

of

variance in the insulin-dependent patients was from 7.5% to 8.8% with repeated measurements. In longitudinal studies with several measurements the mean coefficient of variances varied between 7.4% and 3.4%. In the non-insulin-dependent patients the coefficient of variances between two tests were 7.0% and 5.3% for normoalbuminuric and microalbuminuric patients, respectively. In cross-sectional studies as well as in longitudinal studies, it has been consistently shown that GFR is well preserved and at a supranormal level in patients with normoalbuminuria

and

microalbuminuria. A decline in GFR appears to start around the transition from microalbuminuria to overt diabetic **renal disease**, although more detailed studies are needed to support this finding. With regard to intervention trials, several studies document that microalbuminuria can be reduced by effective antihypertensive treatment, particularly with angiotensin-converting enzyme inhibitors, also in patients with normal or close to normal blood pressure. Preliminary results from long-term studies suggest that reduction in

microalbuminuria

in these patients is associated with preservation of GFR and, thus, apparently renoprotection. In patients with overt **renal disease**, it has been consistently shown that antihypertensive treatment reduces albuminuria as well as the rate of decline in GFR. This is also observed with combined treatment regimens, for instance beta blockers or angiotensin-converting enzyme inhibitors combined with diuretics, or the three types of drugs in combination.

=> d ibib 11

L11 ANSWER 11 OF 15 MEDLINE

DUPLICATE 2

ACCESSION NUMBER: 97115942 MEDLINE

DOCUMENT NUMBER: 97115942 PubMed ID: 8957034

TITLE: Effect of ramipril on blood pressure and protein excretion rate in normotensive nondiabetic patients with

proteinuria.

AUTHOR: Toto R D; Adams-Huet B; Fenves A Z; Mitchell H C; Mulcahy W; Smith R D

CORPORATE SOURCE: Department of Internal Medicine, University of Texas Southwestern Medical Center at Dallas, 75235-8856, USA.

CONTRACT NUMBER: MO1-RR006633 (NCRR)

SOURCE: AMERICAN JOURNAL OF KIDNEY DISEASES, (1996 Dec) 28 (6) 832-40.

023 Nuclear Medicine  
028 Urology and Nephrology  
037 Drug Literature Index

LANGUAGE: English  
SUMMARY LANGUAGE: English

# ADONIS - Electronic Journal Services

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|                     |  |
|---------------------|--|
| Article title       | Effect of Low-Dose Ramipril on Microalbuminuria in Normotensive or Mild Hypertensive Non-Insulin-Dependent Diabetic Patients |
| Article identifier  | 0895706195102041   |
| Authors             | Trevisan_R Tiengo_A  |
| Journal title       | American Journal of Hypertension   |
| ISSN                | 0895-7061  |
| Publisher           | Elsevier USA   |
| Year of publication | 1995   |
| Volume              | 8  |
| Issue               | 9  |
| Supplement          | 0  |
| Page range          | 876-883  |
| Number of pages     | 8  |
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| Cost centre         | Development  |
| PCC                 | \$20.00  |
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|    | Type | L # | Hits  | Search Text   | DBs                                   |
|----|------|-----|-------|---|---------------------------------------|
| 1  | BRS  | L1  | 21    | comper.in.  | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 2  | BRS  | L2  | 3271  | 435/5.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 3  | BRS  | L3  | 3921  | 435/4.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 4  | BRS  | L4  | 1229  | 435/28.ccls.  | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 5  | BRS  | L5  | 818   | 424/130.1.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 6  | BRS  | L6  | 350   | 424/9.2.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 7  | BRS  | L7  | 2279  | 530/300.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 8  | BRS  | L8  | 412   | 530/303.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 9  | BRS  | L9  | 421   | 530/344.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 10 | BRS  | L10 | 173   | 530/359.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 11 | BRS  | L11 | 338   | 530/362.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 12 | BRS  | L12 | 493   | 530/363.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 13 | BRS  | L13 | 931   | 530/380.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 14 | BRS  | L14 | 303   | 530/382.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 15 | BRS  | L15 | 224   | 530/386.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 16 | BRS  | L16 | 133   | 530/392.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 17 | BRS  | L17 | 123   | 530/394.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 18 | BRS  | L18 | 1605  | 530/395.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 19 | BRS  | L19 | 1389  | 530/399.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 20 | BRS  | L20 | 1023  | 530/413.ccls.   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 21 | BRS  | L21 | 16701 | 12 or 13 or 14 or 15 or<br>16 or 17 or 18 or 19 or<br>110 or 111 or 112 or 113<br>or 114 or 115 or 116 or<br>117 or 118 or 119 or 120 | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 22 | BRS  | L22 | 2     | 121 and 11  | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 23 | BRS  | L23 | 3     | lysosome and 11   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 24 | BRS  | L24 | 56122 | albumin   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 25 | BRS  | L25 | 2074  | lysosome  | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 26 | BRS  | L26 | 23    | 124 same 125  | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 27 | BRS  | L27 | 4459  | 124 same fragment   | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |
| 28 | BRS  | L28 | 3     | 127 same 125  | USPAT; US-PGPUB;<br>EPO; JPO; DERWENT |



|    | Time Stamp       | Comments | Error Definition | Errors |
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| 2  | 2002/09/05 09:27 |          |                  | 0      |
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| 9  | 2002/09/05 09:28 |          |                  | 0      |
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| 19 | 2002/09/05 09:29 |          |                  | 0      |
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| 25 | 2002/09/05 09:31 |          |                  | 0      |
| 26 | 2002/09/05 09:32 |          |                  | 0      |
| 27 | 2002/09/05 09:32 |          |                  | 0      |
| 28 | 2002/09/05 09:32 |          |                  | 0      |

|    | Type | L # | Hits  | Search Text                    | DBs                                |
|----|------|-----|-------|--------------------------------|------------------------------------|
| 29 | BRS  | L29 | 16354 | (kidney or renal) with disease | USPAT; US-PGPUB; EPO; JPO; DERWENT |
| 30 | BRS  | L30 | 778   | 129 same hormone               | USPAT; US-PGPUB; EPO; JPO; DERWENT |
| 31 | BRS  | L31 | 124   | 130 same insulin               | USPAT; US-PGPUB; EPO; JPO; DERWENT |
| 32 | BRS  | L32 | 1     | 131 same albumin               | USPAT; US-PGPUB; EPO; JPO; DERWENT |
| 33 | BRS  | L33 | 10751 | 129 same treat\$4              | USPAT; US-PGPUB; EPO; JPO; DERWENT |
| 34 | BRS  | L34 | 1303  | 133 same protein               | USPAT; US-PGPUB; EPO; JPO; DERWENT |
| 35 | BRS  | L35 | 31    | 134 same albumin               | USPAT; US-PGPUB; EPO; JPO; DERWENT |
| 36 | BRS  | L36 | 9     | 134 same ace                   | USPAT; US-PGPUB; EPO; JPO; DERWENT |

|    | Time Stamp       | Comments | Error Definition | Errors |
|----|------------------|----------|------------------|--------|
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| 32 | 2002/09/05 09:35 |          |                  | 0      |
| 33 | 2002/09/05 09:35 |          |                  | 0      |
| 34 | 2002/09/05 09:35 |          |                  | 0      |
| 35 | 2002/09/05 09:40 |          |                  | 0      |
| 36 | 2002/09/05 09:41 |          |                  | 0      |

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, DRUGU, SCISEARCH' ENTERED AT  
12:02:11 ON 05 SEP 2002

|     |  |
|-----|--|
| L1  | 477 S (COMPER, W?)/AU                  |
| L2  | 342237 S (KIDNEY OR RENAL) (S) DISEASE |
| L3  | 40 S L1 AND L2                         |
| L4  | 21 DUP REM L3 (19 DUPLICATES REMOVED)  |
| L5  | 51295 S ACE INHIBITOR                  |
| L6  | 4159 S L2 AND L5                       |
| L7  | 2928 S L2 (P) L5                       |
| L8  | 242 S L7 AND ALBUMIN                   |
| L9  | 16 S L8 AND RAMIPRIL                   |
| L10 | 10 DUP REM L9 (6 DUPLICATES REMOVED)   |